

AMENDMENTS IN THE CLAIMS

Claims 41-46, 49-51, 56, 58, 59, 61, 63-73, 75, and 77-82 are pending in this application.

Claims 41, 58, 59, 66, and 80-82 are being amended, and new claims 83-86 are being added.

After the amendments, claims 41-46, 49-51, 56, 58, 59, 61, 63-73, 75, and 77-86 will be pending.

Listing of Claims:

1.-40. (Canceled)

41. (Currently amended) A method of treating a subject having a cell proliferative disorder comprising:

- a) contacting the subject with a therapeutically effective amount of a retrovirus, comprising:
  - a retroviral GAG protein;
  - a retroviral POL protein;
  - a retroviral envelope;
  - an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' end of the retroviral genome, ~~wherein a tissue-specific promoter sequence is contained within the LTR sequences at the 5' or 3' or 5' and 3' end of the oncoretroviral polynucleotide sequence;~~
  - a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous nucleic acid encodes a suicide gene; and
  - cis-acting nucleic acid sequences involved in ~~for~~ reverse transcription, packaging and integration in a target cell,
- in a pharmaceutically acceptable carrier; and
- b) contacting the subject with a prodrug which is activated by the expression of the suicide gene;

wherein the cell proliferative disorder is a neoplastic disorder or associated with an overgrowth of connective tissue.

42. (Original) The method of claim 41, wherein the subject is a mammal.
43. (Original) The method of claim 42, wherein the mammal is a human.
44. (Original) The method of claim 41, wherein the contacting is by in vivo administration of the retrovirus.
45. (Original) The method of claim 44, wherein the in vivo administration is by systemic, local, or topical administration.
46. (Withdrawn) The method of claim 41, wherein the contacting is by ex vivo administration of the retrovirus.
47. (Canceled)
48. (Canceled)
49. (Previously presented) The method of claim 41, wherein the oncoretroviral polynucleotide sequence is selected from the group consisting of murine leukemia virus (MLV), Moloney murine leukemia virus (MoMLV), Gibbon ape leukemia virus (GALV) and Human Foamy Virus (HFV).
50. (Previously presented) The method of claim 49, wherein the MLV is an amphotropic MLV

51. (Previously presented) The method of claim 63, wherein the ENV protein is selected from the group consisting of murine leukemia virus (MLV) ENV protein and vesicular stomatitis virus (VSV) ENV protein.
- 52.-55. (Canceled)
56. (Previously presented) The method of claim 41, wherein the cell proliferative disorder is selected from the group consisting of lung cancer, colon-rectum cancer, breast cancer, prostate cancer, urinary tract cancer, uterine cancer lymphoma, oral cancer, pancreatic cancer, leukemia, melanoma, stomach cancer and ovarian cancer.
57. (Canceled)
58. (Currently amended) The method of claim 41, wherein the LTR of the retrovirus comprises a tissue-specific promoter sequence ~~is associated with a growth regulatory gene.~~
59. (Currently amended) The method of claim 41 ~~58~~, wherein the tissue-specific promoter sequence is associated with probasin or a growth regulatory gene.
60. (Canceled)
61. (Previously presented) The method of claim 41, wherein the suicide gene is a thymidine kinase or a purine nucleoside phosphorylase (PNP).
62. (Canceled)
63. (Previously presented) The method of claim 41, wherein the retroviral envelope comprises a chimeric protein.

64. (Previously presented) The method of claim 63, wherein the chimeric protein comprises an ENV protein and a targeting polypeptide.
65. (Previously presented) The method of claim 64, wherein the targeting polypeptide is an antibody, a receptor, or a receptor ligand.
66. (Currently amended) A method of treating a subject having a cell proliferative disorder comprising:
- a) contacting the subject with a therapeutically effective amount of a recombinant retroviral polynucleotide, comprising:
    - a polynucleotide sequence encoding a GAG protein;
    - a polynucleotide sequence encoding a POL protein;
    - a polynucleotide sequence encoding a retroviral envelope;
    - an oncoretroviral polynucleotide sequence comprising a Long Terminal Repeat (LTR) at the 5' and 3' end of the oncoretroviral polynucleotide sequence, ~~wherein a target-specific promoter sequence is contained within the U3 region of the LTR sequences at the 5' or 3' or 5' and 3' end of the oncoretroviral polynucleotide sequence;~~
    - a heterologous polynucleotide sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous polynucleotide encodes a suicide gene;
    - and
    - cis acting nucleic acid sequences involved in reverse transcription, packaging and integration in a target cell; and
  - b) contacting the subject with a prodrug which is activated by the expression of the suicide gene;  
wherein the cell proliferative disorder is a neoplastic disorder or associated with an overgrowth of connective tissue.
67. (Previously presented) The method of claim 66, wherein the polynucleotide sequence encoding a retroviral envelope encodes a chimeric protein.

68. (Previously presented) The method of claim 67, wherein the chimeric protein comprises an ENV protein and a targeting polypeptide.
69. (Previously presented) The method of claim 68, wherein the targeting polypeptide is an antibody, a receptor, or a receptor ligand.
70. (Previously presented) The method of claim 66, wherein the GAG, POL and retroviral envelope polynucleotide sequences are from murine leukemia virus (MLV) or Moloney murine leukemia virus (MoMLV).
71. (Previously presented) The method of claim 70, wherein the MoMLV is an amphotropic MoMLV.
72. (Previously presented) The method of claim 68, wherein the ENV protein is an ecotropic protein.
73. (Previously presented) The method of claim 68, wherein the ENV protein is selected from the group consisting of a murine leukemia virus (MoMLV) ENV protein and vesicular stomatitis virus (VSV) ENV protein.
74. (Canceled)
75. (Previously presented) The method of claim 66, wherein the suicide gene encodes a thymidine kinase or a purine nucleoside phosphorylase (PNP).
76. (Canceled)

77. (Previously presented) The method of claim 66, wherein the regulatory nucleic acid sequence operably linked with the heterologous nucleic acid sequence is selected from the group consisting of a promoter, an enhancer, and an internal ribosome entry site.
78. (Previously presented) The method of claim 66, wherein the polynucleotide sequence is contained in a viral particle.
79. (Previously presented) The method of claim 66, wherein the polynucleotide sequence is contained in a pharmaceutically acceptable carrier.
80. (Currently amended) A method of treating a subject having a cell proliferative disorder comprising:
- a) contacting the subject with a therapeutically effective amount of a recombinant replication competent murine leukemia virus (MLV), comprising:
    - an MLV GAG protein;
    - an MLV POL protein;
    - an MLV envelope;
    - an MLV polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' end of the MLV polynucleotide sequence, ~~wherein a target-specific promoter sequence is contained within the LTR sequences at the 5' or 3' or 5' and 3' end of the MLV polynucleotide sequence,~~
    - a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous nucleic acid encodes a suicide gene; and
    - cis-acting nucleic acid sequences necessary for reverse transcription, packaging and integration in a target cell; and
  - b) contacting the subject with a prodrug which is activated by the expression of the suicide gene;
- wherein the cell proliferative disorder is a neoplastic disorder or associated with an overgrowth of connective tissue.

81. (Currently amended) A method of treating a subject having a cell proliferative disorder comprising:
- a) contacting the subject with a therapeutically effective amount of a recombinant replication competent retrovirus comprising:
- a retroviral GAG protein;
  - a retroviral POL protein;
  - a retroviral envelope comprising a chimeric env protein comprising a targeting ligand;
  - an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' end of the oncoretroviral polynucleotide sequence, ~~wherein a tissue-specific promoter sequence is contained within the U3 region of the LTR sequences at the 5' or 3' or 5' and 3' end of the oncoretroviral polynucleotide sequence,~~
  - a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous nucleic acid encodes a suicide gene; and
  - cis-acting nucleic acid sequences involved in reverse transcription, packaging and integration in a target cell; and
- b) contacting the subject with a prodrug which is activated by the expression of the suicide gene;
- wherein the cell proliferative disorder is a neoplastic disorder or associated with an overgrowth of connective tissue.
82. (Currently amended) A method of treating a subject having a cell proliferative disorder comprising:
- a) contacting the subject with a therapeutically effective amount of a recombinant retroviral polynucleotide, comprising:
- a polynucleotide sequence encoding a GAG protein;
  - a polynucleotide sequence encoding a POL protein;
  - a polynucleotide sequence encoding a retroviral envelope, wherein said envelope comprises a chimeric env protein comprising a targeting ligand;

an oncoretroviral polynucleotide sequence comprising a Long Terminal Repeat (LTR) at the 5' and 3' end of the oncoretroviral polynucleotide, ~~wherein a tissue-specific promoter sequence is contained within the U3 region of the LTR sequences at the 5' and/or 3' end of the oncoretroviral polynucleotide;~~  
a heterologous polynucleotide sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous polynucleotide encodes a suicide gene;  
b) ~~—~~ cis acting polynucleotide sequences involved in reverse transcription, packaging and integration in a target cell; and  
e) b) contacting the subject with a prodrug which is activated by the expression of the suicide gene;  
wherein the cell proliferative disorder is a neoplastic disorder or associated with an overgrowth of connective tissue.

83. (New) A method of treating a subject having a cell proliferative disorder comprising: contacting the subject with a therapeutically effective amount of a retrovirus, comprising:
- a retroviral GAG protein;
  - a retroviral POL protein;
  - a retroviral envelope;
  - an oncoretroviral polynucleotide sequence comprising long-terminal repeat (LTR) sequences at the 5' and 3' end of the retroviral genome;
  - a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous nucleic acid encodes a cytokine or an anti-angiogenic factor; and
  - cis-acting nucleic acid sequences necessary for reverse transcription, packaging and integration in a target cell,
- in a pharmaceutically acceptable carrier;  
wherein the cell proliferative disorder is a neoplastic disorder or associated with an overgrowth of connective tissue.



84. (New) The method of claim 83 wherein the cytokine is selected from the group consisting of interleukins 1 through 12, interferons, tumor necrosis factor (TNF) and granulocyte-macrophage-colony stimulating factor (GM-CSF).
85. (New) The method of claim 83 wherein the cytokine is interleukin 2.
86. (New) The method of claim 83 wherein the cytokine is GM-CSF.